



MSX1 gene

msh homeobox 1

Normal Function

The *MSX1* gene provides instructions for making a protein that regulates the activity of other genes. The *MSX1* gene is part of a larger family of homeobox genes, which act during early development to control the formation of many body structures. Specifically, this gene is critical for the normal development of the teeth and other structures in the mouth. It may also be important for development of the fingernails and toenails.

Health Conditions Related to Genetic Changes

Wolf-Hirschhorn syndrome

The *MSX1* gene is often deleted in people with Wolf-Hirschhorn syndrome, even though it is located outside the region of chromosome 4 that is typically deleted in people with this condition. A loss of the *MSX1* gene probably disrupts the regulation of several other genes, particularly genes involved in the development of the mouth and teeth. Researchers believe that a deletion of the *MSX1* gene disrupts the formation of oral structures in early development, leading to missing teeth and other dental abnormalities. A loss of the *MSX1* gene probably also causes an opening in the roof of the mouth (cleft palate) and/or a split in the upper lip (cleft lip) in some people with Wolf-Hirschhorn syndrome.

other disorders

Changes in the *MSX1* gene are also associated with other abnormalities of mouth and tooth development. For example, changes in this gene contribute to some cases of cleft lip and/or cleft palate in people who do not have Wolf-Hirschhorn syndrome. These genetic variations (polymorphisms) have been associated with isolated cleft lip and cleft palate in several different populations worldwide. *MSX1* polymorphisms appear to be one of many genetic and environmental factors that play a role in oral clefting.

At least six *MSX1* mutations are responsible for oligodontia, a condition in which multiple teeth fail to develop. Some individuals with *MSX1* mutations have a combination of oligodontia and cleft lip and/or cleft palate. Mutations in the *MSX1* gene likely reduce the amount of functional MSX1 protein within cells, which disrupts the early development of structures in the mouth.

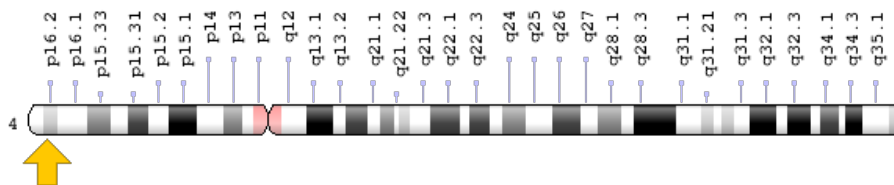
Another mutation in the *MSX1* gene has been found to cause Witkop syndrome (also known as tooth-and-nail syndrome) in one large family. This rare condition

is characterized by a variable number of missing teeth and abnormalities of the fingernails and toenails. The *MSX1* mutation responsible for Witkop syndrome, written as Ser202Ter or S202X, leads to the production of an abnormally short, nonfunctional version of the MSX1 protein. A loss of this protein disrupts the formation of the teeth and nails during early development.

Chromosomal Location

Cytogenetic Location: 4p16.2, which is the short (p) arm of chromosome 4 at position 16.2

Molecular Location: base pairs 4,859,665 to 4,863,936 on chromosome 4 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- homeobox 7
- homeobox protein MSX-1
- HOX7
- HYD1
- msh homeo box 1
- MSH Homeo Box Homolog 1 (Drosophila) Gene
- msh homeobox homolog 1
- MSX1_HUMAN
- OFC5

Additional Information & Resources

GeneReviews

- Wolf-Hirschhorn Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1183>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28MSX1%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- MUSCLE SEGMENT HOMEBOX, DROSOPHILA, HOMOLOG OF, 1
<http://omim.org/entry/142983>
- OROFACIAL CLEFT 5
<http://omim.org/entry/608874>
- TOOTH AGENESIS, SELECTIVE, 1
<http://omim.org/entry/106600>
- WITKOP SYNDROME
<http://omim.org/entry/189500>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_MSX1.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=MSX1%5Bgene%5D>
- HGNC Gene Family: NKL subclass homeoboxes and pseudogenes
<http://www.genenames.org/cgi-bin/genefamilies/set/519>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7391
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/4487>
- UniProt
<http://www.uniprot.org/uniprot/P28360>

Sources for This Summary

- Hu G, Vastardis H, Bendall AJ, Wang Z, Logan M, Zhang H, Nelson C, Stein S, Greenfield N, Seidman CE, Seidman JG, Abate-Shen C. Haploinsufficiency of MSX1: a mechanism for selective tooth agenesis. *Mol Cell Biol*. 1998 Oct;18(10):6044-51.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/9742121>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC109190/>
- Jezewski PA, Vieira AR, Nishimura C, Ludwig B, Johnson M, O'Brien SE, Daack-Hirsch S, Schultz RE, Weber A, Nepomucena B, Romitti PA, Christensen K, Orioli IM, Castilla EE, Machida J, Natsume N, Murray JC. Complete sequencing shows a role for MSX1 in non-syndromic cleft lip and palate. *J Med Genet*. 2003 Jun;40(6):399-407.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12807959>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735501/>
- Jumlongras D, Bei M, Stimson JM, Wang WF, DePalma SR, Seidman CE, Felbor U, Maas R, Seidman JG, Olsen BR. A nonsense mutation in MSX1 causes Witkop syndrome. *Am J Hum Genet*. 2001 Jul;69(1):67-74. Epub 2001 May 16.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11369996>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1226049/>
- Kim JW, Simmer JP, Lin BP, Hu JC. Novel MSX1 frameshift causes autosomal-dominant oligodontia. *J Dent Res*. 2006 Mar;85(3):267-71.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16498076>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2238638/>
- Lidral AC, Reising BC. The role of MSX1 in human tooth agenesis. *J Dent Res*. 2002 Apr;81(4):274-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12097313>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2731714/>
- Modesto A, Moreno LM, Krahn K, King S, Lidral AC. MSX1 and orofacial clefting with and without tooth agenesis. *J Dent Res*. 2006 Jun;85(6):542-6.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16723652>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2241923/>
- Mostowska A, Kobiela A, Trzeciak WH. Molecular basis of non-syndromic tooth agenesis: mutations of MSX1 and PAX9 reflect their role in patterning human dentition. *Eur J Oral Sci*. 2003 Oct;111(5):365-70. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12974677>
- Nieminen P, Kotilainen J, Aalto Y, Knuutila S, Pirinen S, Thesleff I. MSX1 gene is deleted in Wolf-Hirschhorn syndrome patients with oligodontia. *J Dent Res*. 2003 Dec;82(12):1013-7.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14630905>
- Vastardis H, Karimbux N, Guthua SW, Seidman JG, Seidman CE. A human MSX1 homeodomain missense mutation causes selective tooth agenesis. *Nat Genet*. 1996 Aug;13(4):417-21.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/8696335>
- van den Boogaard MJ, Dorland M, Beemer FA, van Amstel HK. MSX1 mutation is associated with orofacial clefting and tooth agenesis in humans. *Nat Genet*. 2000 Apr;24(4):342-3. Erratum in: *Nat Genet* 2000 May;25(1):125.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10742093>

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